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D-7800 / LINURON SR

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Linuron Rat Study - Evaluation of Hematological Measure - HB (g %)

Caswell No. 528

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On the basis of the memorandum on Linuron, Comments on Statistical Reevaluation of Blood Data from the 2-year Rat Study (B. Fisher and B. Litt December 3, 1986), Dr. Rowe suggested that a reanalysis with time periods up to 12 months would be sufficient to establish any potential compound-related hemotoxicity. Thus, the previous problem of animal substitutions in the 2-year time period would be eliminated since during the first year, the hemotological readings were based on the same set of 10 animals at 3, 6, and 12-month time intervals. In addition, Dr. Rowe suggested that the reevaluation of the hemoglobin (g %) measures alone would be sufficient to identify hemotoxicity.

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Attachment to D-7799A. 6 pages

Consequently, this selected blood compound measure in both sexes was evaluated by means of a SAS-ANOVA computer program.

The structure of this model for ANOVA analysis assumed that the dose and time variables were fixed conditions, and that the number of animals (10) in each dose-time category represented repeat independent measurements (which were considered to be a nested effect sample).

It was also assumed that DuPont conducted this study by taking and measuring blood components for all dose levels at each time period in a random manner, so that a day-to-day time bias would not be inadvertently built into the values.

The results of the ANOVA analysis of hemoglobin measures (g %) in both sexes indicated that time was an important effect, regardless of dose levels (see Graph 1 and 2).

In males, the overall dose comparisons, confounded by time, were not significantly different. In addition, the pairwise comparisons of control with each of the dose levels, made by the use of the Least Significant Difference method, also showed no significant differences (see Table 1 for details).

In females, the time factor interaction with dose was highly significant ($p < .01$). Thus the overall comparisons of dose were inappropriate and indicated that pairwise comparisons with control should be calculated separately for each time period. The statistical method, Duncan's test, showed that both in the 6-month and 12-month data, there was statistical significant ($p < .05$) evidence of a difference between the controls and the higher dose (625 ppm) reading of HG (g %). While for the ~~3-month and~~ 12-month data there was a statistically significant ($p < .05$) difference between the control and the mid-dose (125 ppm) group (see Table 2 for details).

In conclusion, only the pairwise comparisons of controls and the low dose (50 ppm) in both sexes for the aforementioned time periods showed no statistically significant differences.

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Table 1

Linuron Rat Study - Males - Hemoglobin (g %); ANOVA Results

Hemoglobin (g %) - Means+				
	Months			
Dose ppm	3	6	12	Total Time (Average)
0	16.35	15.53	15.53	15.80
50	16.05	15.08	15.10	15.41
125	16.61	15.50	15.45	15.85
625	16.63	14.93	14.94	15.50

Table 2

Linuron Rat Study - Females - Hemoglobin (g %); ANOVA Results

Hemoglobin (g %) - Means+				
	Months			
Dose ppm	3	6	12	Total Time (Average)
0	15.36	15.22	15.52	15.37
50	15.82	14.94	15.34	15.37
125	15.19	14.95	14.66*	14.93
625	15.38	14.17*	13.74*	14.43

+ Mean value based on 10 animals.

Significant differences among all dose groups denoted at Control. Significant differences in pairwise comparison denoted at Dose level.

* $p < .05$
** $p < .01$

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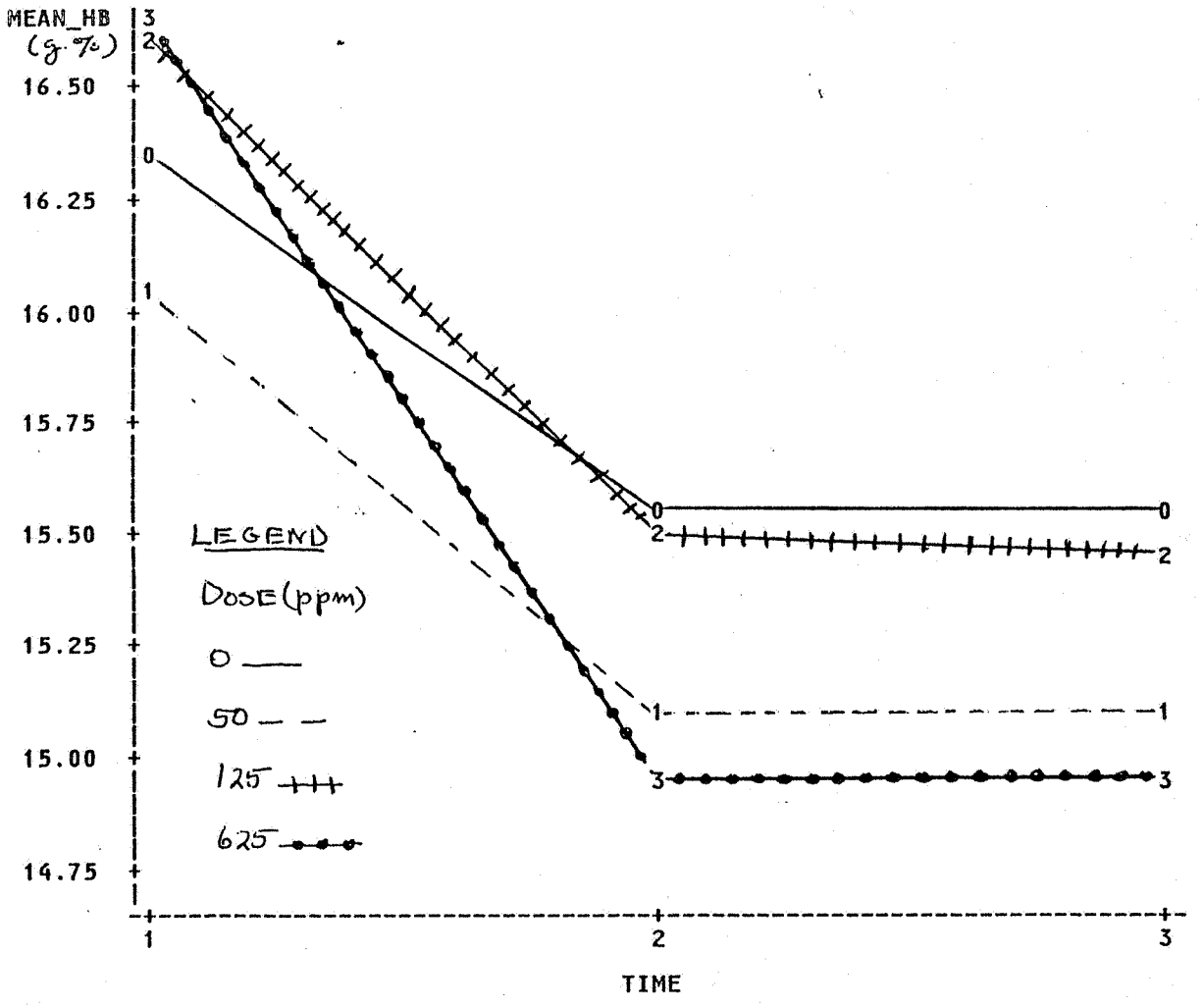
References

Fisher, R.A. (1942) The Design of Experiments, third edition, Edinburgh: Oliver and Boyd.

Snedecor, G.W.; Cochran, W.G. (1967) Statistical Methods, sixth edition, Ames, Iowa: The Iowa State University Press.

Graph 1. — LINURON, CHRONIC RAT STUDY, MALE - HB MEASURES

PLOT OF MEAN_HB*TIME SYMBOL IS VALUE OF DOSE



Graph 2. — LINURON, CHRONIC RAT STUDY, FEMALES- HB MEASURES

PLOT OF MEAN_HB*TIME SYMBOL IS VALUE OF DOSE